Amendments to the Claims:

Please cancel claims 45, 46, without prejudice or disclaimer.

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-43 (previously canceled)

44. (Previously presented) A transgenic mouse having a genome comprising human heavy and light chain immunoglobulin variable region gene loci, wherein the human heavy and light chain variable region loci replace mouse endogenous heavy and light chain immunoglobulin variable region gene loci, and the human heavy and light chain variable region loci are linked to endogenous mouse heavy and light chain immunoglobulin constant region gene loci to form hybrid loci, whereby the hybrid loci rearrange during B-cell development such that the mouse produces a serum containing an antibody comprising human heavy and light chain immunoglobulin variable regions and mouse heavy and light chain immunoglobulin constant regions in response to antigenic stimulation.

45-46. (cancel)

47. (currently amended) The transgenic mouse of claim 44, ~~45 or 46~~ wherein the endogenous light chain immunoglobulin constant region gene locus is a kappa light chain.

48-52. (previously canceled)

53. (currently amended) The transgenic mouse of claim 44 ~~or 45~~, wherein the endogenous light chain immunoglobulin constant region is a lambda light chain region.

54. (new) The transgenic mouse of claim 44, wherein the mouse has heavy and light chain immunoglobulin variable region loci that are entirely human linked to heavy and light chain immunoglobulin constant region loci that are entirely mouse to form the hybrid loci.

55. (new) A method of producing an antibody, comprising

providing a transgenic mouse having a genome comprising human heavy and light chain immunoglobulin variable region gene loci, wherein the human heavy and light chain variable region loci replace mouse endogenous heavy and light chain immunoglobulin variable region gene loci,

and the human heavy and light chain variable region loci are linked to endogenous mouse heavy and light chain immunoglobulin constant region gene loci to form hybrid loci, whereby the hybrid loci rearrange during B-cell development such that the mouse produces a serum containing an antibody comprising human heavy and light chain immunoglobulin variable regions and mouse heavy and light chain immunoglobulin constant regions in response to antigenic stimulation

stimulating the mouse with an antigen;

preparing a hybridoma expressing the antibody from the mouse.

56. (new) The method of claim 55, further comprising preparing a human antibody comprising the human heavy and light chain immunoglobulin variable regions.

57. (new) The method of claim 56, wherein the human antibody further comprises human heavy and light chain constant regions.

58. (new) A method of producing an antibody, comprising

providing a transgenic mouse having a genome comprising human heavy and light chain immunoglobulin variable region gene loci, wherein the human heavy and light chain variable region loci replace mouse endogenous heavy and light chain immunoglobulin variable region gene loci, and the human heavy and light chain variable region loci are linked to endogenous mouse heavy and light chain immunoglobulin constant region gene loci to form hybrid loci, whereby the hybrid loci rearrange during B-cell development such that the mouse produces a serum containing an antibody comprising human heavy and light chain immunoglobulin variable regions and mouse heavy and light chain immunoglobulin constant regions in response to antigenic stimulation

stimulating the mouse with an antigen;

isolating DNA encoding the heavy and light chain variable regions of the antibody from the mouse;

operably linking the DNA encoding the variable regions to DNA encoding human heavy and light chain constant regions

expressing a human antibody comprising the human heavy and light chain variable regions and the human heavy and light chain constant regions.